

Validity of ejection fraction as a measure of myocardial functional state: impact of asynchrony

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KEYWORDS

- Left ventricle;
- Ejection fraction;
- Regional wall motion;
- Mechanical asynchrony;
- Ultrasound examination;
- 3D reconstruction

Aims The goal of this study was to test whether peculiarities of left ventricular (LV) regional function place limits on the validity of ejection fraction (EF) as a measure of the myocardial functional state.

Methods and results Transthoracic and transoesophageal data from patients with a variety of cardiac conditions were used for analysis of LV regional function. The focus was on the effects of mechanical asynchrony. Ejection fraction was calculated on the basis of LV end-diastolic volume and end-systolic volume obtained by two different ways: (i) end-systolic volume as a whole; and (ii) the sum of all regional end-systolic volumes (which may occur at different times). The relative difference, D-EF, between EFs obtained by (i) and (ii) was taken as the 'merit' of EF. A value of zero is the highest merit. Irrespective of the examination method, we found that D-EF was always higher than zero, and that its value depended on the extent of mechanical asynchrony.

Conclusions Ejection fraction is not the arithmetic average of regional EFs. An increase of asynchrony increases D-EF, i.e. it reduces the merit of EF as a measure of cardiac function.

Introduction

Left ventricular ejection fraction (LVEF), which is a non-dimensional quantity that is defined as LV stroke-volume divided by the end-diastolic volume, multiplied by 100%, reflects the ability of the LV to eject blood. Since this mainly depends on myocardial function, EF serves as an indirect measure of LV contractile state as a whole.

At the same time, LVEF is the result of regional function. Theoretically, the contributions of all myocardial regions to the EF should be the same when there is LV functional (mechanical) homogeneity. In that case, LVEF is equal to any regional EF (r-EF) and, therefore, LVEF is 100% a reflection of the myocardial functional state. Meanwhile, even in the normal LV, regional myocardial function is non-uniform, depending on local peculiarities of LV wall structure.¹⁻³

In pathological states, disease impairs myocardial structure and function dynamically and unequally, resulting in some degree of mechanical asynchrony.⁴⁻⁷ In general, asynchrony implies differences in time course of contraction between

different LV wall regions. In the pathological state, asynchrony may be a reflection not only of abnormalities in the LV conduction system but also myocardial ischaemia or damage.⁸⁻¹¹

The presence of mechanical asynchrony implies that the time course of local ejection during the cycle may differ in different regions. In that case, LVEF defined at the end of systole is not equal to the arithmetic average of all r-EFs. Therefore, LV asynchrony may influence the EF value as a measure of overall myocardial functional state.

In this paper, we present evidence that the merit of EF as a measure of the overall functional state depends on the extent of mechanical asynchrony. We present data from patients with a variety of cardiac conditions, obtained by transthoracic (TTE) and transoesophageal (TEE) ultrasound. Using regional LV wall-motion analysis of single long-axis sections and with LV 3D reconstruction, we show that LVEF merit as a reflection of myocardial functional state as a whole depends on the peculiarities of LV regional function.

Methods

This investigation conforms to the principles outlined in the Declaration of Helsinki. Transoesophageal echocardiographic data from 10

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r-EF of these regions differs from r-EF at end-systole of LV as a whole.

Figure 4 illustrates these variables for a representative patient. Regional EFs measured at regional end-systole and at LV end-systole are plotted. The numbers of frames where individual r-EF were obtained are marked on the top of every column. One can see the variations of time points with RMS value of 48.4 ms (At). Furthermore, r-EFs defined on the basis of regional ESV are greater than r-EFs calculated at LV end-systole. As a consequence, the st -EF

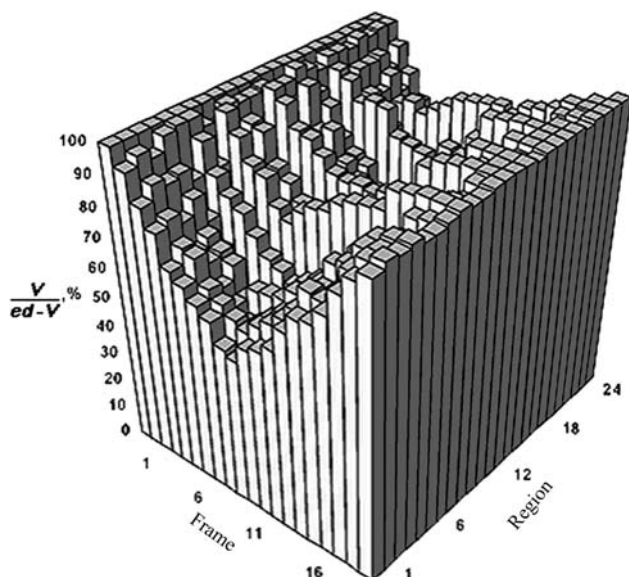


Figure 3 Left ventricular regional volume changes during a cardiac cycle assessed by 3D reconstruction. One hundred per cent on the ordinate corresponds to regional end-diastolic volume.

is less than the an -EF (41 and 45%, respectively). The D-EF for this case is equal to 9%.

Qualitatively similar results were obtained with TTE studies of LV regional function analysis of LV long-axis views. The area dynamics of 12 LV sectors during the cardiac cycle in a patient with IHD (HYHA III) is presented in Figure 5. Figure 6 shows the r-EF distribution in the same way as presented in Figure 4. In this case, $As = 34\%$, $At = 56$ ms, st -EF = 37%, an -EF = 43%, and the D-EF was 11%.

Table 1 lists the mean values of asynchrony parameters, LVEF, and D-EF, obtained both by TEE and by TTE. In general, both methods showed large variations in all parameters. At the same time, mean values of st -EF for both TEE and TTE were less than those for an -EF (for TEE $P > 0.05$, for TTE $P < 0.05$).

A close correlation was found between the asynchrony parameters and the EF relative difference. For TEE, the correlation coefficients between D-EF and As and D-EF and At were: 0.59 ($n = 10$, $P = 0.052$) and 0.73 ($n = 10$, $P < 0.05$); for TTE, they were 0.67 ($n = 40$, $P < 0.001$) and 0.69 ($n = 40$, $P < 0.001$), respectively.

Figures 7 and 8 show the graphical presentation of the relationships between D-EF and As for TEE data, and D-EF and At for TTE data, respectively. The data show that increases of spatial asynchrony resulted in increases of EF relative difference, i.e. in a diminution of EF merit. Time asynchrony influenced ID-EF in the same way as spatial asynchrony.

Close negative correlation between the EF relative difference and the st -EF was seen as well. The correlation coefficients for TEE and TTE were: -0.69 ($n = 10$, $P < 0.05$) and -0.78 ($n = 40$, $P < 0.001$), respectively. Negative correlation implies the lower the LVEF, the higher the D-EF. In

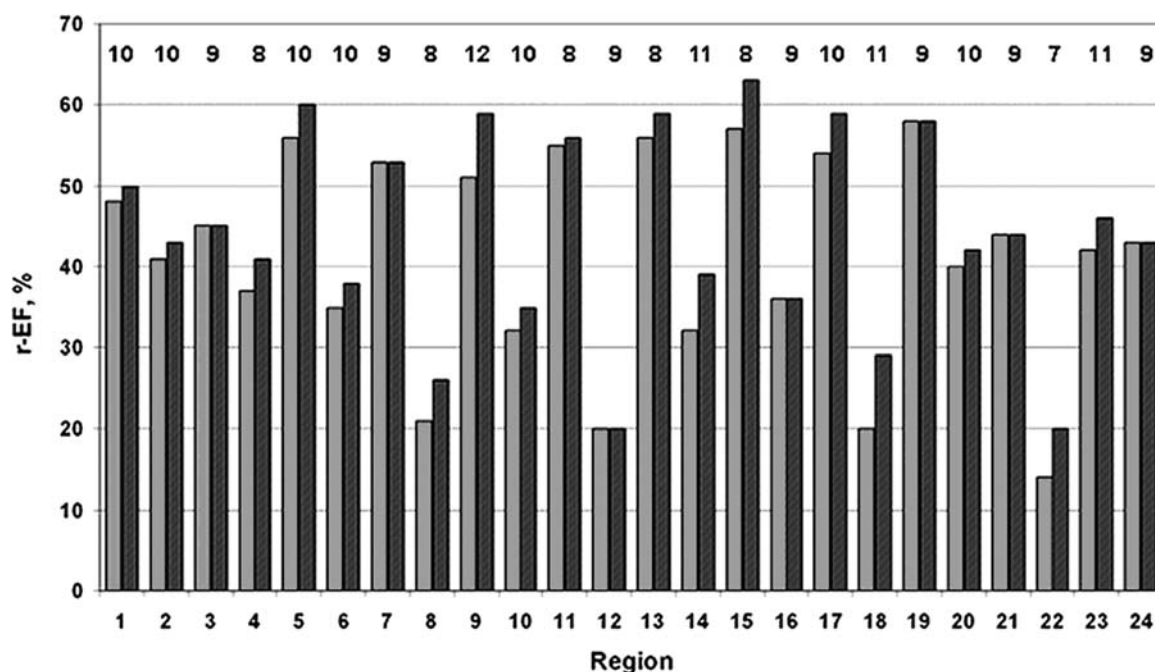


Figure 4 Regional ejection fraction (r-EF) distribution assessed by 3D reconstruction at end-systole of each region and end-systole of the left ventricle. Lighter columns correspond to r-EFs obtained at end-systole of the left ventricle. Number of frame where regional end-systolic volume was calculated is marked on the top of each column. (See text for further explanation.)

contractile properties of LV regions. In other words, the arithmetic average of r-EFs should be equal or at least close to global EF. Indeed, although regional contributions to LVEF at the end-systole differed substantially, an arithmetic average of r-EF was close to global EF (*Figures 2, 4, and 6*). However, when considering regional dynamics (*Figure 3*), it is apparent that some regional ESVs occurred at different times during the cycle, and with lower volumes compared with their volumes at LV end-systole. Therefore, r-EF is not the same as it is at LV end-systole. As a result, the LV *an*-EF is higher than *st*-EF.

On the one hand, myocardial function is based on muscular contractility, commonly taken as the ability to generate tension and the ability to shorten. On the other hand, at a given level of contractility, muscular function depends on loading conditions, i.e. sarcomere pre- and after-load. At LV end-diastole, myocytes in different wall regions have different loads and different initial lengths. For example, even in the normal LV, wall stress increases towards the endocardium,²¹ and initial sarcomere lengths are greater in the endocardium than in the epicardium.²² During systole, regional shortening and wall thickening are controlled mainly by myocyte after-load and instantaneous length. At a given level of contractility, those values depend on regional morphology and initial loading conditions.^{2,21,23,24} These factors play an important role in regional loading profiles, resulting in load and length redistributions among fibre layers and regions during the cardiac cycle. These redistributive features are amply demonstrated in experiments using the interaction model of two cardiac muscles connected in parallel or series.^{7,25}

Thus, the pattern of LV regional function is complex and closely depends on regional myocardial contractility and structure. Differences in LV regional function commonly manifest as mechanical asynchrony, i.e. differences of mechanical behaviour at the same point of time. In the pathological state, disease may bring increased LV asynchrony. Hence, given the high level of asynchrony existing at LV end-systole, LVEF merely reflects the LV's ability to eject blood, and not the true state of myocardial function. In other words, the more the mechanical asynchrony, the less the merit of LVEF as a measure of the myocardial functional state.

Both time and space asynchrony varied substantially among patients (*Table 1*). Independently of the aetiology of disease, our results showed that increased asynchrony resulted in an increase of the EF-difference measure. Therefore, an increase of asynchrony brought a decrease of EF merit. Importantly, the effect of asynchrony on the D-EF does not depend on LVEF measurement accuracy. We found close correlation between D-EF and asynchrony parameters (As and At) using both 3D reconstruction and LV long-axis views (*Figures 7 and 8*).

We conclude, therefore, that LV mechanical asynchrony decreases EF merit. The quantitative value of D-EF depends on the degree of asynchrony. In relatively healthy subjects, mechanical asynchrony is minimal: As varies in the range of 5–15% and At 10–35 ms.^{7,26} Hence, D-EF for the normal state is less than that for the pathological state, where D-EF depends on how the pathology affects regional myocardial contractility and/or structure. Thus, many methodical and clinical factors may influence the merit of LVEF as a measure of the myocardial functional state.

Finally, we discuss potential clinical applications of the D-EF calculation. In context of this study, patients were not selected by aetiology. On the contrary, we took video records of a continuous string of patients in order to demonstrate the usefulness of the approach for routine clinical practice. At the same time, we may suggest some speculation on the basis of the data obtained.

First, consider D-EF from another point of view, say, as a possible measure of myocardial functional reserve. The presence of mechanical asynchrony compromises LV pump function. Indeed, the contribution of cardiac wall regions to LV stroke-volume is not necessarily maximal at LV end-systole (*Figures 4 and 6*). Therefore, some potential for LV pump reserve may be assumed. According to the close correlation between D-EF and *st*-EF, the lower the ability of LV to eject the blood, the more the functional reserve. Hence, at low values of LVEF, some increase of LV stroke-volume could be envisioned if dynamic function of all regions could somehow be synchronized.

Generally, there are two ways of reducing mechanical asynchrony. One is a change in regional contractility and the other is a variation in regional loading profiles. For example, in patients with dilated cardiomyopathy and left bundle-branch block, cardiac resynchronization therapy (CRT) results in an increase of LV function by means of electrical synchronization. In spite of the absence of any direct effect of CRT on contractility, the positive influence of cardiac pacing on LV function is associated with a change of wall-loading conditions. As we demonstrated earlier, successful CRT manifests itself as an increase of LVEF, a decrease of asynchrony, and a reduction in D-EF as well.²⁷ This result implies that CRT releases myocardial functional reserve.

Unfortunately, the prognostic value of D-EF could not be estimated in the above-mentioned study²⁷ because the study was based on a limited number of observations on several patients only. Meanwhile, we believe that obtaining values of D-EF may help predict good responders to CRT. Since the extent of mechanical asynchrony reflects the level of development of many cardiovascular diseases, D-EF may be an additional useful measure for monitoring both the myocardial functional state and the results of treatment.

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